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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/216,609 12/21/98 HANSEN

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HM22/0214

EXAMINER

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HOLLERAN, A	
ART UNIT	PAPER NUMBER

1642
DATE MAILED:

02/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/216,609

Applicant(s)

Hanson, H.J.

Examiner

Anne Holleran

Group Art Unit

1642

☒ Responsive to communication(s) filed on Nov 20, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1035 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-54 is/are pending in the application.

Of the above, claim(s) 47 and 48 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-7, 11-18, 20, 22, 23, 31-34, 36, 39, 42-46, and 49-54 is/are rejected.

☒ Claim(s) 8-10, 19, 21, 24-30, 35, 37, 38, 40, and 41 is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

1. This Office Action is responsive to the Request for Reconsideration filed November 20, 2000.

Claims 1-54 are pending.

Claims 47 and 48, drawn to non-elected species, are withdrawn from consideration.

Claims 1-46 and 49-54 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

3. The instant application claims priority, as a continuation-in-part, to copending application 08/445,110 (now U.S. Patent 5,851,527) filed May 19, 1995, which was a continuation of 07/182,623 (now abandoned) filed Apr. 18, 1988. The following claims of the instant application are drawn to inventions that are not supported by the disclosure of 08/445,110: claims 7-10, 12-15, 19, 21-30, 35, 37, 38, 40, 41, 45, 47, 48 and 54. For comparison with the prior art the filing date of the instant application, Dec. 21, 1998, will be used.

Claim Rejections Withdrawn:

4. The rejection of claims 1-50, 53 and 54 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of Applicant's persuasive arguments.

5. The rejection of Claims 1-54 under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement commensurate with the scope of the claimed invention is withdrawn in view of Applicant's persuasive arguments.

6. The rejection of claims 1, 2, 4, 5, and 53 under 35 U.S.C. 103(a) as being unpatentable over Bagshawe et al (Bagshawe, K.D. et al, Br. J. Cancer, 58: 700-703, 1988; IDS ref. "A21") in view of Martinis et al (supra) and further in view of Goldenberg (U.S. Patent 4,624,846, published Nov. 25, 1986) is withdrawn in view of the fact that the Bagshawe et al reference does not antedate the effective filing date of claims 1, 2, 4, 5 and 53.

Claim Rejections Maintained:

6. The rejection of Claims 1-6, 11, 12, 16-18, 20, 31-34, 36, 39, 42-44, 46, 49-53 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of U.S. Patent No. 5,851,527 is maintained. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-6, 11, 12, 16-18, 20, 31-34, 36, 39, 42-44, 46, 49-53 are drawn to methods that are broader in scope than the methods

claimed in U.S. Patent No. 5,851,527. Applicant provided no arguments in response to the double-patenting rejection.

Claims 1-6, 11, 12, 16-18, 20, 31-34, 36, 39, 42-44, 46, 49-53 of the instant application are drawn to methods which may or may not comprise administration of clearing agents. To the extent that claims 1-6, 11, 12, 16-18, 20, 31-34, 36, 39, 42-44, 46, 49-53 read on methods that do not employ clearing agents the claims of the instant application are anticipated by the subject matter of the claims of U.S. Patent No. 5,851,527. To the extent that claims 1-6, 11, 12, 16-18, 20, 31-34, 36, 39, 42-44, 46, 49-53 read on methods that do employ clearing agents, the claims of the instant application would be obvious over the subject matter of the claims of U.S. Patent No. 5,851,527 as evidenced by the disclosure of 5,851,527 (column 13, lines 44-56). Both sets of claims read on methods, kits and preparations useful for targeting cytotoxic agents to a target site.

7. The rejection of Claim 54 under 35 U.S.C. 102(b) as being anticipated by Bosslet et al (Bosslet, K. Cancer Research, 54, 2151-2159, 1994; IDS ref. "A29") is maintained.

Applicant's arguments were considered but not found persuasive. Applicant argues that rejection over Bosslet et al should be withdrawn because claim 54 should be accorded the effective filing date of April 18, 1988. Applicant points to a passage in the grandparent application (07/182,623) and asserts that this passage provides support for the specific embodiment of a protein-enzyme conjugate comprising a fusion protein of the targeting protein and the enzyme. This is not found persuasive because the passage only teaches a general covalent linkage between an antibody and an enzyme but does not provide support for the specific species

of a fusion protein between a targeting protein and an enzyme or between an antibody and an enzyme. The rejection is maintained for the reasons of record.

8. The rejection of claims 12, 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sharma et al (Sharma, S.K. et al, Br. J. Cancer, 61: 659-662, 1990; IDS ref. "A28") in view of Martinis et al. (WO 83/03679, published Oct. 27, 1983) is maintained.

Applicant's arguments were considered but not found persuasive. Applicant argues that the combined references do not teach each and every element of the claimed inventions.

Applicant states that the teachings of Martinis et al do not suggest or teach the use of bispecific antibodies which bind to an enzyme but instead only teach bispecific antibodies which bind to therapeutic agents. However, the teachings of Martinis et al are relied upon to demonstrate that it was known in the art to use bispecific antibodies to target a cytotoxic agent to a target site as an alternative to targeting a cytotoxic agent which is chemically conjugated to an antibody.

Nothing in the teachings of Martinis et al excludes the possibility that the "cytotoxic agent" is an enzyme. A cytotoxic agent is any agent that may be used to cause cytotoxicity. Applicant has failed to show that Martinis et al teaches away from using a bispecific antibody to target an enzyme to a target site. Applicant has failed to show that the binding of an antibody to an enzyme as means for targeting an enzyme to a target site. In addition, the prior art as a whole teaches the claimed invention because Sharma et al teaches methods of targeting prodrugs to a target site where an enzyme activates the prodrug and Martinis et al provides the teaching that bispecific

antibodies are useful as connector between a targeting agent and a cytotoxic agent. Thus, the rejection is maintained for the reasons of record.

9. The rejection of Claims 12, 14 and 15 under 35 U.S.C. 103(a) as being unpatentable over Blakey et al (Blakey, D.C. et al, Cancer Res. 56: 3287-3292, 1996) in view of Martinis et al. (WO 83/03679, published Oct. 27, 1983) is maintained for the reasons of record and for the reasons stated above for the rejection of claims 12, 14, 15 over Sharma et al in view of Martinis et al. Applicant's arguments in response to the rejection over the combination of Blakey et al and Martinis et al were presented together with the arguments in response to the rejection of the combination of Sharma et al with Martinis et al.

10. The rejection of Claims 12, 14, 15 under 35 U.S.C. 103(a) as being unpatentable over Bagshawe et al (Bagshawe, K.D. et al, Br. J. Cancer, 58: 700-703, 1988; IDS ref. "A21") in view of Martinis et al (supra) and further in view of Goldenberg (U.S. Patent 4,624,846, published Nov. 25, 1986) is maintained for the reasons of record and for the reasons stated above with regard to the teachings of Martinis et al.

New Grounds of Rejection:

x. Claims 22 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22 is vague and indefinite because the phrase “the enzyme to which is attached at least one oligomer to which is conjugated...” lacks antecedent basis in either claim 17 or claim 1.

Claim 23 is vague and indefinite because it is not clear whether both substances are present at the target site.

7. Claims 7 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Potter et al (Potter, P.M. et al. Cancer Research, 58(16): 3627-3632, 1998, August; abstract only) in view of either Bosslet, Sharma et al or Blakey et al and further in view of Martinis et al.

Claims 7 and 45 are drawn to methods of targeting a therapeutic agent to a target site comprising administering a targeting compound, administering an enzyme and administering a prodrug, where the prodrug is CPT-11 and, for claim 7, the enzyme is an esterase. For claim 45, CPT-11 is converted to camptothecin.

Potter et al teach that CPT-11 is a prodrug that is activated by the action of carboxylesterases and teach a recombinantly produced version of the enzyme and that CPT-11 is toxic to cells expressing and secreting a carboxylesterase. Potter et al do not teach a method of in vivo administration of either a targeted enzyme or CPT-11. However, targeting enzymes to target sites is well known in the art as evidenced by the teachings of either Bosslet, Sharma et al or Blakey et al. Furthermore, as discussed above the teachings of Martinis can be used to modify the methods of targeting enzymes to target sites by using bispecific antibodies to target the enzymes to target sites instead of using covalent modification of an antibody to carry the enzyme to a target site. Thus, it would have been obvious to one of skill in the art at the time the

invention was made to have combined the teachings of the prior art and have made the methods of either claims 7 or claim 45 which require the use of CPT-11 and an esterase as the specific prodrug and enzyme. One would have had a reasonable expectation of success in using CPT-11 and the carboxylesterase of Potter et al because Potter et al teaches that lipid bilayer association is not required for substrate metabolism and because Potter et al teaches which modifications of the enzyme result in a functional enzyme and which do not.

Conclusion

No claim is allowed. Claims 8-10, 19, 21-30, 35, 37, 38, 40, 41 are objected to for depending from rejected claims. This action is not made final.


Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892.

Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Anne L. Holleran
Patent Examiner
February 12, 2001


ANTHONY C. CAPUTA
PATENT EXAMINER
TECHNOLOGY CENTER